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Two sets of goals were accomplished. 1) *Neurophysiological studies* were conducted that indicated that sensory input to primary somatosensory (SI) cortical neurons is "gated" during behavior. This occurs in some regions of SI but not in others. Quantitative estimates of this gating under different behavioral circumstances are provided. Equations are described which predict the magnitude of the premovement activity during vibratory triggered trials from the vibratory responsiveness of the neurons and the amount of premovement activity exhibit in visually cued trials. 2) In *Psychophysical studies* reaction times (RTs) of monkeys and human subjects were determined for ballistic or targeted wrist flexion and extension movement made in response to visual and vibratory go-cues. The RT experiments indicated that humans and monkeys make ballistic movements more quickly (50-100 msec) in response to vibratory as compared to visual signals. Human subjects also make movements more quickly to a visual target if, in addition to target presentation, a vibratory cue is also given. The psychophysical studies suggest that there is a performance benefit in using tactile in addition to visual cues to control behavior. The neurophysiological studies indicate ways in which the brain processes the somatosensory component of information used in controlling goal-oriented behavior.

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Introduction

The overall goal of the research conducted by this laboratory is to understand the role that behavioral contingencies play in modulating the responsiveness of SI neurons during the initiation and execution of sensory-triggered wrist movements. A secondary goal has been to understand the functional differences of neurons located in the regions that comprise SI during these movements. Advances toward these goals make two contributions; the first to our general understanding of how the primate nervous system functions and the second to practical applications for device control. These two contributions are closely interrelated.

Observations concerning the function of the macaque sensorimotor system during controlled wrist movement are readily generalizable to humans since it has been shown that the detection thresholds for tactile events are remarkably similar in monkeys and human. Thus, a knowledge of how sensory responsiveness is modulated when monkeys perform wrist movements will give an indication of the capacities of the human nervous system under similar behavioral conditions.

With this knowledge, more efficient device control mechanisms involving wrist movement can be designed. In instances in which a subject is required to maintain visual fixation upon a myriad of indicators and in which any auditory signals might interfere with communication, vibratory warning signals may prove beneficial. They may signal important events without requiring a substantial attentional shift away from other (visual and/or auditory) tasks in which the subject is engaged.

Two types of studies were conducted under the auspices of AFOSR GR 88-0179. 1) *Neurophysiological studies* were conducted to determine whether sensory input to primary somatosensory (SI) cortical neurons is "gated" during behavior. It was found that input was gated in a predictable and reproducible manner in some regions of SI but not in others. Quantitative estimates of this gating under different behavioral circumstances were derived by constructing models and applying them to the neurophysiological data. 2) In *Psychophysical studies* reaction times (RTs) and movement times (MTs) of monkeys and human subjects were determined for ballistic or targeted wrist flexion and extension movement made in response to visual and vibratory go-cues. The RT experiments indicated that humans and monkeys make ballistic movements more quickly (50-100 msec) in response to vibratory as compared to visual signals. Subjects also make movements more quickly to a visual target if, in addition to target presentation, a vibratory cue is also given. Human subjects under these conditions have quicker RTs while the MTs are not different. Nor does there appear to be any difference in accuracy or percentage of correct trials. The psychophysical studies suggest that there is a performance benefit in using tactile in addition to visual cues to control behavior. The neurophysiological studies indicate ways in which the brain processes the somatosensory component of information used in controlling goal-oriented behavior.

Experimental Design and Methods - Animal.

Results from the experiments described below, designed to demonstrate the modulation of responsiveness of SI neurons, indicate that a significant percentage of these neurons show markedly different response profiles associated with the behavioral context in which peripheral stimuli are delivered and wrist movements made. Alterations in responsiveness appear to be related to whether or not monkeys make movements in response to sensory inputs that are delivered to the same body part that is subsequently moved and whether a reward for these movements is predictable. Other SI neurons are characterized by decreases or increases in firing rates that occur before movement onset and before changes in EMG activity, suggesting that the modulatory influences that contribute to these altered discharge rates are centrally rather than peripherally generated. These centrally generated influences may be different depending upon receptive field (RF) type, handle loading conditions and the direction of movement with respect to the stimulated surface of the hand. Three types of experiments were conducted to gain additional information about changes in SI neuronal responsiveness in monkeys. Moreover, behavioral testing was done with human volunteers trained to perform two types of reaction time wrist movement tasks under varying conditions to determine the performance advantages of using vibratory signals during goal-oriented behavior.

First, the general features of the monkey tasks will be described, followed by a description of the surgical and recording procedures, the procedures for data collection and analysis, and then by the procedures for histology and penetration reconstruction. Next, the specific tasks to be used with monkeys are described in detail followed by the specializations involved with the human psychophysical experiments.

General Experimental Methods - Monkey Training and Surgery.

Adult rhesus monkeys *(Macaca mulatta)* were trained to perform a stereotyped sequence of behaviors while seated in a Plexiglas™ monkey chair. The monkeys were cared for in accordance with the *NIH Guide for Care and Use of Laboratory Animals, revised 1985*. Each monkey's forearm was restrained just above the wrist and at the elbow with velcro straps. Each animal palm manipulated a smooth aluminum plate attached at one end to the axle of a brushless DC torque motor (Vernitron, VBTMH38-B1, see [18]). The angular deflection of the plate was displayed to the monkeys by a row of 31 light-emitting diodes (LEDs). The central LED, signifying the centered position of the plate, was different from the remainder in both size and color.

Behavioral tasks for each investigation are described below. Upon successful completion of a rewarded trial, fruit juice or water was given to the previously fluid deprived animals. The body weight of each animal was monitored and care was taken to supplement the experimental fluid intake to maintain the animal at 90% of the normal body weight. On days when the animals did not perform, water was available in their cages.

After an animal attained a reliable task performance, surgery was be performed at the University's Animal Resources Division under the direction of the University's Veterinary staff. Monkeys were be maintained at a surgical level of anesthesia with a mixture of oxygen and nitrous oxide along with Halothane. Proper facilities for artificially respirating the animals and monitoring expired carbon dioxide were available as needed and the animal's electrocardiogram was monitored. A scalp incision was made and the temporalis muscle reflected over the region of the left parieto-frontal cortices. A craniotomy was performed so that a passivated stainless steel recording chamber could be implanted over the craniotomy [31, 75]. This chamber was constructed from a single block of 316-L stainless steel and had an internal diameter of 18mm in the short dimension and was 36mm in length. This recording cylinder was similar to those previously in use in the Laboratory of Neurophysiology at the National Institute of Mental Health. This design has proven to be adequate for the investigation of both cortical and subcortical structures. The chamber was stereotaxically placed over the skull at an angle of 45° from true horizontal, with its anterior

margin located at AP +14.5, centered at LM +15. Based on the published coordinates and experience, this should allow for access to the somatosensory cortex. In addition, stainless steel skull bolts were implanted at four sites and used for head restraint during recording sessions. The chamber and the bolts were secured to the skull with dental acrylic (Howmedica Surgical Simplex P).

The wound was closed in layers after incisions were made to allow the chamber and the bolts to pass through the scalp. Topical antibiotics were applied to the wound margin. Systemic antibiotics were given following surgery and a small amount of intrathecal strength Chloramphenicol was put in the sealed chamber to guard against infection. Complete blood counts were done to monitor the animal's progress. Care was taken to eliminate any possible pain experienced by the monkeys.

Electrophysiological recording sessions.

Recording electrodes were fabricated by placing platinum-iridium wire in 28-gauge hypodermic tubing and then placing that inside another, larger piece of tubing. The first acted to prevent the fine wire from deviating extensively during the course of the penetrations; the second acted to secure the electrode to the chronic microdrive. The platinum-iridium wire were etched to a fine tip of approximately 2-5 μm by passing alternating current through it while it was immersed in a bath of Chlorox or Sodium Cyanide. A relatively coarsely tapered electrode profile was necessary for the transdural penetration used in these experiments. These electrodes were coated with molten glass distally and Epoxylite- (Epoxylite International) proximally. The tip of the electrode was exposed electrically by pulsing a DC voltage across the tip.

During each recording session the glass-coated platinum-iridium microelectrode were positioned over the pre- or postcentral cortex by means of microdrive with a x-y stage (Narishige MO-95B) attached to the saline-filled sealed chamber. The electrode was manually advanced to the dural surface and then to the cortical surface. This initial depth of the cortex was used later in the reconstruction of penetration sites. The electrode was advanced in small increments into the ipsilateral cortex.

Extracellular recordings of the activity of single cortical neurons were made while the monkeys perform behavioral tasks in a manner similar to that used in other investigations to examine the overlying cortical regions. Recording sessions normally lasted between 1-3 hours and were immediately terminated if the animal showed any signs of discomfort or did not perform the task. Experience over the last nine years has indicated that monkeys routinely perform for this duration and are highly motivated. As warranted, the recording sites were micro-stimulated (train of 11 cathodal pulses; 200 μsec pulse duration at 330Hz, intensity <=60 μA, one train per sec for at least 1 minute) to determine if there are noticeable microstimulation effects.

Before and after each session, the recording chamber was flushed with sterile saline. After recording, the chamber was filled with saline, antibiotics added, and the chamber sealed with a teflon cap. The monkeys were then be returned to their home cages.

Data Collection and Analysis.

The electrical activity of single neurons located in the primary somatosensory cortices was recorded during the performance of behavior tasks by the monkeys. The potentials recorded by the platinum-iridium microelectrodes were routinely amplified and filtered and displayed on an oscilloscope. The oscilloscope was triggered by the initially negative unitary potentials associated with neural spikes recorded at a safe distance from the soma. The spikes of individual neurons were discriminated using a time-amplitude window discriminator after the signal had been delayed to allow viewing of the entire waveform.

Data were collected by an on-line data collection routine for real-time events that is run by a PDP-11/23+ microcomputer. Discriminator pulses corresponding with single neuronal spikes were entered into the data stream via parallel input lines (DRV-11), interrupting the computer and causing the real-time clock to be read (Data Translations DT 2769) so that the time of occurrence is recorded with resolution of 100

microseconds. The analog signal corresponding to the handle position and hence the location of the animal's hand was sampled at a rate of up to 400Hz, with 100Hz the typical sampling frequency, by an A/D converter (Data Translations DT 2781). The computer, which controled the behavioral paradigm, also entered information about the execution of the task in real-time, coding each unique event and branch point decision and entered these into the data stream. At regular intervals, EMG recordings of the forearm muscles acting across the wrist were made, sometimes simultaneously with cortical recordings. Intramuscular EMG wires (stranded stainless, teflon insulated; Bergen Wire Rope Co.) were temporarily implanted in muscles using sterile 25 gauge needles as guides. The EMG activity was rectified, integrated and then digitized by the on-line data collection routine. As always, the goal will be to correlate neural activity with specific behavioral and stimulation parameters.

Once the activity of each neuron had been recorded during the performance of the appropriate behavioral task, the possible peripheral RFs of the neuron were determined by probing the skin with a Rowan anesthesiometer, palpating bellies and manipulating joints.

After each recording session, an off-line data analysis and display routine was run for the recordings of each neuron. This program allowed the simultaneous video graphic display (Matrox, MLSI-512, NEC Multisync Monitor) of digitized neural events and the analog records of the behavior and allowed paper copies of the display to be made with a line printer so that changes in neuronal firing rate could be correlated with changes in hand position.

Data analysis was conducted in several stages. Graphic and numerical displays of the neuronal activity and wrist position were reconstructed by an off-line data analysis routine. Perievent histograms, raster displays of the neuronal activity, and analog displays of the animal's behavioral performance also were examined. These displays were oriented in time either with the onset of the sensory stimulus or with the onset of the sensory-triggered movements. The level of background activity for each set of trials was determined by finding the mean discharge rate during the hold period (measured in spikes/s) and was compared to the mean discharge rate of neuronal activity during all subsequent phases of the task that preceded movement. Neuronal activity associated with the onset of vibratory stimuli was measured by determining the first monotonic change in activity after stimulus onset in which the magnitude of the change was at least ±50% of the background activity for at least 30 consecutive msec. Premovement activity was measured from displays centered on movement onset using the same temporal and magnitude criteria. Premovement activity was considered to be the first change in activity following the return to background after the vibratory response and continuing until movement onset. Stimulus-related and premovement activity changes were compared by subtracting the background activity from each. RTs were calculated in monkey and human experiments as the time from go-cue onset to the time of the first detectable change in wrist position. In some human experiments, MTs (from movement onset to target attainment) were calculated.

Histology and Penetration Reconstruction.

At the end of the final recording session, each animal was anesthetized with ketamine hydrochloride and a microelectrode placed in the cortex, in turn, at each of several points of interest. Small electrolytic lesions were made at each point of interest by passing anodal current (10μA, 5-10 sec) through the recording electrode. After the animal recovered from the anesthesia, it was allowed to survive for 1-2 days. Then the animal was given a lethal dose of Pentobarbital and perfused intracardially with saline followed by 10% buffered formol saline. During the perfusion, a set of four pins was advanced into the brain parallel to the electrode tracts through guides in a specially designed chamber cap. Once perfusion was completed, the pins were removed. The brain was removed from the skull, and cut on a freezing microtome in 50 μm sections in a sagittal plane.

The location of penetrations and of recording sites within each tract were determined by considering a number of factors. Photographs of the surface of the experimental hemisphere were taken and the location

of each penetration estimated by reference to the location of marking pin tracks made at known chamber positions. Enlarged scale drawings of each brain section containing a penetration tract were made using a microprojector. The location of each tract was usually evident in histological material. Each recording site was located by computing the recording site depth from surface along the penetration tract as reconstructed on scaled drawings of the histological material and correcting for any shrinkage by adjusting the scale by the difference in the distance between the marking lesions tracks before and after embedding and sectioning the material.

Every attempt was made to determine from which cytoarchitectonic region each recording was made by comparing each site with the morphological characteristics of the somatosensory cortical areas by criteria established previously . In this way, the functions of each of the cytoarchitectonic regions that comprise the primary somatosensory cortices could evaluated by the response of their neurons recorded during the performance of the behavior tasks.

Behavioral Paradigms.

These studies used behavioral paradigms which consisted of three basic parts: the maintenance of an initial wrist position, the detection of a go cue delivered and ballistic wrist flexion or extension movements (Figure 1). The manipulandum was placed directly beneath the wrist joint thus allowing, when necessary, flexion and extension of the pronated hand about the wrist. A constant torque of approximately 0.07 Newton-meters (Nm) was applied in the upward direction requiring the animals to exert a flexion force to maintain the plate in a centered position corresponding to neither flexion nor extension of the wrist. Each trial was begin when the monkey positioned the handle in the centered zone, thus holding the handle in that position against a small upward force generated by a DC torque motor. A constant force of approximately 0.07 newton-meters was generated by the motor (Vernitron model VBTMH38-B1) which will be under feedback control by circuitry that controls the motor's power supply (Kepco BOP 36-5M). The position of the handle attached to the axle of the torque motor was sensed by a rotary variable differential transformer (RVDT - Pickering model 23380) in series with the motor's axle. Visual feedback of the handle position was displayed to the monkey by the LED panel described above with the central LED, corresponding to the centered handle position, different in color and size from the remaining LEDs. The feedback system was calibrated so that each successive LED above or below the center lamp was illuminated for a 1° change in handle position in that direction from the center zone.

The monkey held this centered position for an interval without moving. This hold time was pseudo-randomly vary, based on the output of a computer random number generator, but was always 0.5, 0.75, 1.0, 1.25 or 1.5 sec. If the animal moved prior to the completion of the hold period, the trial was cancelled. The monkey could initiate a new trial by returning the handle to the central zone.

Two types of go-cues were used in each block of trials during the two tasks. Each trial began when the monkey centered the handle, thereby illuminating the central LED. The handle had a load which provide a constant torque of 0.07Nm assisting extension movements. At the start of each trial, a combination of two instruction LEDs was sometimes presented. The LEDs were located in the upper left corner of the visual display (11.8° of visual angle from the center). The presence or absence of illumination of each LED instructed the monkey about the direction of the required movement (a red LED on means extension and off means flexion) and the type of sensory stimulus that would be presented in that trial (a green LED on meant visual and off meant vibratory). These LEDs also warned the monkey that a trial had started. The monkey maintained a centered wrist position for 0.5, 1.0, 1.5 or 2.0sec. The hold time for each trial was obtained from a computer algorithm, running in real-time, that produced a uniform distribution of the four periods. Autocorrelation analysis indicated that there was no statistically significant sequential structure to the output of this pseudo-random number generating algorithm. If the monkey maintained a steady position within ±0.5° (each lamp =1°) of center, a vibratory or visual stimulus was presented and the current wrist position was designated as the start position for analysis.

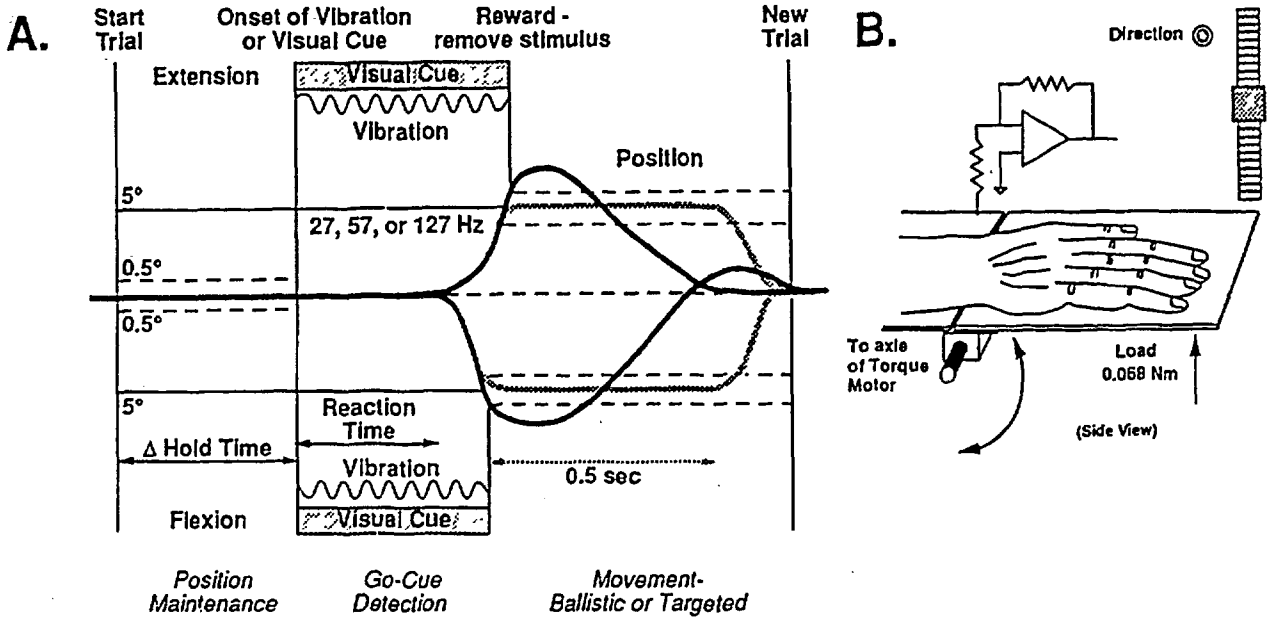


Figure 1. (A) Schematic of basic paradigms. Each task consists of three parts: wrist position maintenance, go-cue detection and wrist movement. Hold time duration (0.5-1.5 sec) and cue type are randomized. During the unexpected failure paradigm, monkey made ballistic wrist movements >5° from center in response to vibratory go-cues and sometimes receive a reward. Each monkey's hand was pronated (B) and movements were made against a load assisting extension movements. Human subjects placed their hands on a handle as in (B). The upwardly directed load was 0.12Nm and they made wrist movements of fixed amplitude to a target (grey lines in A) depending the position of that target. The first human psychophysical experiment determined the relationship between RT for visual cued or vibratory cued trials (see text). The second determined the relationships between RT and movement times for visual only and combined cue trials when movements were made to a target 5° located from center (see text).

Vibratory cues consisted of vibrating the handle by driving the motor with a low-amplitude sine wave (<0.057° or less than 100 μm peak-to-peak measured 10cm distal to the coupling of the handle to the motor). This amplitude was sufficient to excite cutaneous receptors in the palm and fingers. Three stimulation frequencies were tested; 27, 57 and 127Hz, which are known to excite cutaneous rapid adaptors, both rapid adaptors and Pacinian afferents, and probably only Pacinian afferents, respectively. Higher frequencies are also known to excite muscle spindles. Visual cues consisted of adding or subtracting a DC voltage from the wrist position signal, and resulting in a shift in the illuminated lamp (±2.4° of visual angle from display center; "lamp shift") in the opposite direction from the requested movement by an amount equal to that required to recenter the display (5.0°). Sensory stimuli remained on until the monkey moved at least 5° from the start position. It was determined that the first change in handle position 0.1° from the start position following stimulus onset gave the most reliable indicator of the actual start of the movements. This was designated as the first detectable change in position. Its occurrence after stimulus onset was entered into the data stream. Monkeys received an audible "click" and a fruit juice or a water reward if the movement was made in the appropriate direction. This click informed the monkey that the trial had been successful. It also served as a signal for the monkey to recenter the handle to begin the next trial.

Monkeys were first trained to perform wrist flexion and extension movements in response to vibratory cues only. Once they reached a stable level of performance, they were trained to make wrist movements in response to visual cues as well. After an initial period during which these animals learned to make the appropriate movements in response to either type of cueing stimulus, their performance again stabilized. The ballistic movements made by the monkeys were not be restricted in speed and amplitude other than by stops in the apparatus at ±30° of angular deflection from center. Flexion and extension movements were

requested in alternating blocks of 10 trials each. When both vibratory and visual stimuli were used, they were pseudorandomly distributed within blocks for a given vibratory stimulus frequency and load. Randomization was accomplished with the same computer algorithm described above. Using this basic paradigm, four phenomema were investigated.

Comparison of Premovement Activity

First, we examined the amplitude and timimg of premovement neuronal activity which occurred during vibratory-cued as compare with visually-cued trials. This was done to test the hypothesis that a peripheral stimulus, such as vibration, that may interfere with the sensing of wrist position may invoke stronger sensory gating prior to movement than none interferring stimuli.

Stimulus Response Reactivation

Second, for a specific class of cortical neurons, the quickly adapting neurons, we sought to determine if part of the premovement activity which they expressed was actually a reactivation of the sensory response which was previously turned off. This was done to determine why this class of neurons showed different relationships from all other groups between the premovement neuronal activity which occurred during vibratory-cued as compare with visually-cued trials

Stimulus Response Enhancement and/or Suppression

Third, we examined the magnitude of vibratory stimulus related neuronal activity during blocks of movement trials as compared with blocks of trials in which the animals were instructed withhold movement in response to vibratory stimuli. This was done to determine if SI neurons were more responsive to peripheral stimuli if those stimuli were behaviorally important signals for the initiation of a behavior which leads to a reward as compared with a signal that a reward is forthcoming if no behavioral change occurs. In "no-movement trials" the visual display was blanked and the monkeys held a steady wrist position for a pseudorandomly assisted hold time before the vibratory stimuli were presented for 1 sec. Movement in response to vibratory stimuli during this type of trial cancelled the trial. The animals could reinitiate a trial by once again holding a steady wrist position.

Reward Predictability

Fourth, we sought to determine if reward predictability and hence an animal's expectation influenced SI neuronal sensory responsiveness. The paradigm for this study was similar to those described above, in that the monkeys were required to make ballistic flexion and extension movements of at least 5° after receiving the go-cue. In this experiment the reward schedule for vibratory cued trials was pseudorandomly varied. The monkey in this study performed vibratory-cued wrist flexion and extension movements of at least 5° from center. Correct performance was rewarded only 75% of the time. In the other 25% of the correctly performed trials (pseudo-randomized within blocks), the reward for correct performance was withheld. The monkey began the next trial by returning the handle position to the center zone. Flexion and extension movements were requested in groups of 10 correctly executed trials each. The neuronal activity during rewarded trials were compared with that during trials immediately following a withheld reward for corresponding flexion and extension movements. Temporally and magnitude assessments of stimulus-related and premovement activities were conducted to determine whether these activities were enhanced or suppressed in the rewarded trials as compared with the trials following those that were not rewarded.

Experimental Design and Methods - Human Subjects.

Adult volunteers performed the paradigm described below. They were asked to perform the task with their preferred hand. All had normal or corrected-to-normal vision and normal hearing. These subjects received no compensation for participating in this study.

Subjects were seated in a specially designed chair in a quiet, moderately lit (5 foot-candles) room and view a display panel placed 50cm directly in front of them at eye level. This display contained 31 light-

emitting diodes (LEDs) located behind a smoky-grey acrylic plate. The details of this display are described above. The subject's hand rested on a flat aluminum handle coupled at one end to the axle of a brushless DC torque motor while the forearm was supported by an arm rest.

Behavioral Paradigms for Studies of Reaction Times and Movement Times During Ballistic and During Multimodal vs. Visually Cued Movements

In most respects, the two paradigms used were identical to that described above. In the first paradigm, a vibratory cue or a visual cue consisting of illuminating an LED on the visual display signalled the subject that he or she should make a ballistic flexion or extension movement. In the case of the visually-cued trials the LED illuminated signaled the subject to move in the direction opposite the lamp shift (as described above). The second paradigm, the go cue for movement consisted of the presentation of a visual target alone or the visual target *and* a vibratory stimulus (multimodal cue) delivered to the palm of the hand that is to be moved. Vibratory components consisted of vibrating the handle by driving the torque motor with a low-amplitude sine wave (< 100 μm peak-to-peak measured 10cm from the coupling of the handle to the motor) at either 27, 57, or 127Hz. Visual targets consisted of adding or subtracting a DC voltage from the coupled wrist position signal, resulting in a shift in the illuminated lamp (± 1.7° of visual angle from display center) in the direction from the requested movement (5° of wrist movement; either flexion or extension). Either cue (combined or target only) remained on until the subject moved to align the wrist position cursor with the target on the visual display, holding the handle in the target position for 0.5 sec. In either paradigm, the subjects heard a click if a trial's movement was appropriate. This click informed the subject that the trial was successful and also served as a signal to recenter the handle to begin the next trial. On the first training day each subject was be instructed to make either the ballistic or targeted wrist flexion and extension movements as quickly as possible without sacrificing movement accuracy. The speed and amplitudes of these targeted movements were not restricted other than by stops in the apparatus at ± 30° of angular deflection from center. However, a trial was be considered a failure in the targeted task if the subject "overshot" the target by <1.5° in an attempt to acquire that target, if the subject did not acquired the target within 1sec of movement onset or if the new position was not held for 0.5 sec. Flexion and extension movements were requested in alternating blocks of 10 trials each. The two cue types were randomly presented within blocks for a given vibratory stimulus frequency. Three groups of at least 120 trials were collected daily. The total duration of these manipulations is about 20-30 min.

Reaction Times During Ballistic Movements

This study was undertaken to determine if subjects could make reaction time wrist flexion and extension movements more quickly in response to vibratory as compared with visual go cues. The hypothesis to be tested was that movement would be made more quickly following vibratory cues. Thus the subjects would show a perfomance benefit when using this type of cue.

Reaction Times and Movement Times During Multimodal vs. Visually Cued Movements

This study was undertaken to determine if subjects would still show a perfomance benefit when making 5° targeted movements with the addition of a vibratory cue as compared with the presentation of the target alone. We predicted that subjects reaction times would be faster with the addition of a vibratory signal to the go cue sequence but that their movement times would not be different.

Results

For the past 3 years the P.I., in collaboration with several investigators, has conducted research designed to achieve a better understanding of the functional organization of SI and the roles that neurons in this region play in behavior involving controlled wrist movements. Previous work has yielded an appreciation of elaboration of the complex topographic relationships of the representations of inputs from contralateral parts of the body. These representations appear to reach their most complex form in primates. In other studies, reorganization of SI following peripheral denervation was observed, suggesting that in adult primates the central somatosensory representations are not static but rather dynamically maintained. These earlier investigations raised several questions, including those of etiological nature such as "what is the selective advantage for primates to maintain two essentially cutaneous representations with SI (areas 3b and 1)" and "why should these areas reorganize differently?" It was thought that one reason might be that these areas, along with areas 3a and 2, have unique functional roles in behavior. To study this possibility and because much remained to be known about the functional properties of SI neurons during goal-oriented, sensory-triggered movements, recording experiments in behaving monkeys were conducted.

Sensory Responsiveness During Behavior - Initial Studies

Initial studies were conducted to determine the sensory responsiveness of SI neurons while monkeys performed a paradigm that used palmar vibratory stimuli as go-cue for movements. Of 795 task related SI neurons recorded in three monkeys, 298 responded to vibratory go-cues. Two classes of stimulus related responses were noted. The first class consisted of 122/298 SI neurons that deceased activity in response to vibration (VIB- neurons; Figure 2C). Ninety-six were tested for RFs and 30/96 had cutaneous RFs, 55/96 had deep RFs, and 11 had no discernible RFs. The second class consisted of 176/298 SI neurons that increased discharge in association with vibratory go-cues (VIB+ neurons). Of the 127/176 tested for RFs, 44/127 had cutaneous RFs, 63 had deep RFs and 20 had no discernible RFs. Two special sub-classes of VIB+ neurons were noted. First, the activity of 57/176 VIB+ neurons were entrained to one of the stimulus frequencies (Figure 2A). Second, 75/176 of the VIB+ neurons exhibited profound decreases in discharge before EMG and movement onset, even though the vibratory stimuli were still present and the wrist position had not changed (Figure 2B). This phenomenon was termed "premovement suppression" (PMS), a type of premovement activity. As will be discussed below, premovement activity was not unique to this sub-class. VIB+ premovement suppression neurons were rarely found in area 3b, but were more frequently found in areas 3a, 1 and 2. This work was published during the term of AFOSR GR 88-0217.

Reference: R.J. Nelson. Set related and pre-movement related activity in primate primary somatosensory cortical neurons depends upon stimulus modality and subsequent movement. Brain Res. Bull. 21(3):411-424, 1988.

Additional experiments sought to determine if SI sensory responses were conditionally dependent upon behavior. Two monkeys made vibratory-triggered wrist movements to receive a reward (go-trials) or maintained wrist position and were not rewarded (no-go trials). Of 67 SI neurons tested using these two paradigms, 14/14 area 3a, 1/18 area 3b, 22/32 area 1 and 1/3 area 2 neurons exhibited different activity associated with vibration onset in the two paradigms (Figure 2C&D). This work was published prior to the current or the preceding grant (AFOSR GR 85-0179).

Reference: R.J. Nelson. Responsiveness of monkey primary somatosensory neurons to peripheral stimulation depends on "motor-set". Brain Res., 304:143-148, 1984.

Comparison of Premovement Activity

Non-vibratory responsive SI neurons also exhibit premovement activity. From a population of 619 SI neurons recorded in two monkeys, 103 non-stimulus related neurons were examined because each exhibited a profound increase or decrease in discharge, time-locked with, but occurring 20-170 msec before movement onset (Figure 2E&F). Of these, 19/23 area 3a, 3/18 area 3b, 31/46 area 1 and 10/16

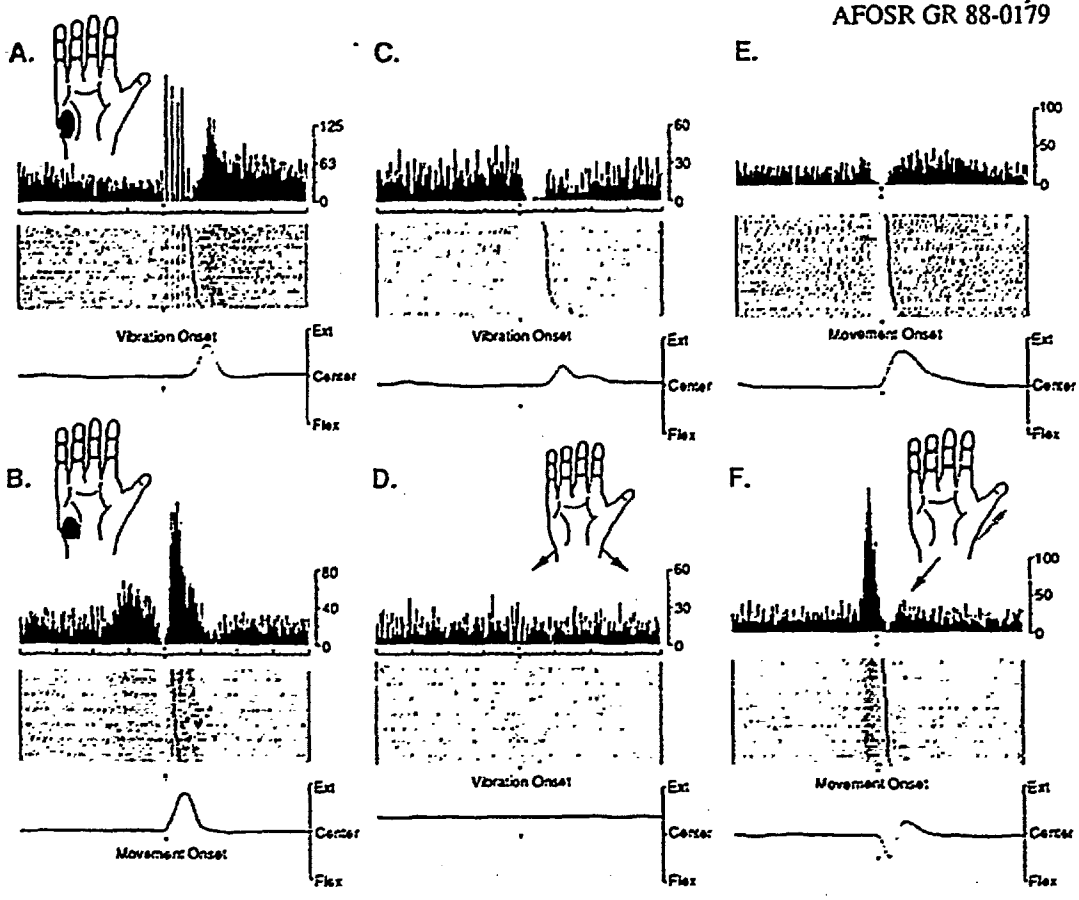


Figure 2 (A-F) Panels consist of 3 displays, above, a peri-event histogram, middle, a raster display where each dot represents a single spike and each row an individual trial, and below, the average positional displacement of all trials. Displays are centered on vibratory stimulus onset (57 Hz, A, C and D) or movement onset (B, E and F). Full span of each display is 2 sec. (A) An area 1 neuron's response to a vibratory go-cue of 27Hz. Dark marks in raster indicate movement onset. Trials are ordered by RT. RF for this neuron was located on the hypothenar pad. (B) Another area 1 neuron with a similar RF. Trials centered on movement onset. Dark marks indicate 5° ballistic movement and reward. Stimulus-related activity (left of arrow) was markedly decreased 80-100 msec before movement onset (premovement suppression). (C) An area 1 neuron exhibiting activity suppression with 57Hz vibratory stimulation as go-cue in movement trials, but not during no-movement trials (D). Neuron responded to radial and ulnar deviation of the wrist. (E&F) Premovement activity of an area 1 neuron that was excited by passive wrist flexion and suppressed by passive wrist extension. This neuron showed no stimulus related activity, but exhibited directional premovement activity 125msec prior to movement onset.

area 2 neurons exhibited premovement activity which was thought to be central rather than peripheral in origin because this activity occurred before task-related EMG activity. As with the observations of PMS for vibratory responsive neurons, early premovement activity rarely was observed in area 3b neurons, but was common for neurons in areas 3a, 1 and 2. Premovement activity in SI neurons was often directional, being of opposite sign preceding flexion as compared with extension movements, although some non-directional responses were noted. This work was published during the preceding grant (AFOSR GR 85-0179).

Reference: R.J. Nelson. Activity of monkey primary somatosensory cortical neurons changes prior to active movement. Brain Res., 406:402-407, 1987.

Experiments were also conducted to determine if premovement activity magnitude is the same when vibration is present as compared to when it is not. If modulation of SI neuronal responsiveness occurs when potentially interfering peripheral stimuli are present, then one would predict that premovement activity in trials triggered by sustained vibration should be less than in trials triggered by visual stimuli. In an initial report, the premovement activity onsets and magnitudes of 53 SI neurons were compared. In general, premovement activity was greater in visually-cued trials as compared with vibratory cued trials. Moreover, for the majority of SI neurons, premovement activity began earlier before movement during

vibratory as compared with visually cued trials. This work was published during the term of AFOSR GR 88-0217.

Reference: R. J. Nelson and V. D. Douglas. Changes in premovement activity in primary somatosensory cortex differ when monkeys make hand movements in response to visual vs. vibratory cues. Brain Res. 484:43-56, 1989.

Stimulus Response Reactivation

In the second study, the activity of 55 area 1 and 19 area 3b neurons with RFs on the hand were examined to determine the onset and magnitude relationships of premovement activity as a function of cortical location, RFs and movement direction. Excluded from this population were SI neurons that had quickly adapting vibratory related responses, for reasons that will be described below. Figure 3, panels A&B, show an example of an area 1 neuron for which premovement activity onset and magnitude during vibratory and visually cued trials were measured. The data were separated into cases by RF type, movement direction and cortical location for reasons explained above. Paired *t*-tests were conducted on the data for each case group. In general, premovement activity during vibratory cued trials occurred 10-40 msec earlier ($p<.01$) before movement than did premovement activity during visually cued trials for area 1 neurons. There were no significant differences in the premovement activity onsets during the two trial types for any of the area 3b case groups. Nor were there any significant differences in premovement activity magnitudes for any of the area 3b groups. However, for area 1 neurons, premovement activity was less in vibratory as compared with visually cued trials ($p<.05$). Scatterplots of the premovement activity magnitudes under the two stimulus-cueing conditions revealed a good linear relationship between these measures over the full range of values recorded (Figure 3C). The slopes of the regressions for all groups of area 1 cases ranged between 0.8-0.9. All slopes were significantly different from 1.0, which would have indicated a unity relationship ($p<.05$; ANOVA).

These results indicate that for area 1, but not area 3b neurons, premovement activity is diminished during trials when potentially interfering (vibratory) peripheral stimuli are present before movement. This suggests that the responsiveness to presumably centrally generated inputs is modulated under these conditions. This modulation is statistically significant, yet falls short of a complete gating of this activity prior to movement.

Area 3b and 1 neurons with quickly adapting (QA) vibratory related responses were analyzed separately. This was done because cluster analysis indicated that QA neurons formed a separate population. QA neurons were also analyzed separately to determine if there was a correlation between the premovement activity and the sensory responsiveness in vibratory cued trials, since the vibratory response was clearly separate from the premovement activity.

Recordings from 166 area 1 and 61 area 3b neurons were initially examined. The recordings were separated into cases by RF type, movement direction and cortical location for the reasons described above. A total of 234/339 (69%) of the area 1 and 94/130 (72%) of the area 3b cases were vibratory responsive. Of these, 133/234 (57%) and 57/94 (61%) area 1 and area 3b cases, respectively, met the remaining selection criteria. A total of 96/133 (72%) of the area 1 and 29/57 (51%) of the area 3b cases recorded from two monkeys had a sufficient number of visually cued trials to enable the determination of premovement activity associated with similar movements made in the absence of vibratory stimuli. Background activity, vibratory response magnitude and premovement activity were calculated for vibratory cued trials (Figure 4A&B). Premovement activity during visually cued trials was also calculated. The vibratory response magnitude for each case group was compared with the premovement activity by Spearman Rank Correlation (Figure 4D). For all area 1 case groups the correlations of these two measures were always significant ($p<=.05$). The vibratory responsiveness and premovement activity of area 3b QA neurons was not correlated ($p<.10$).

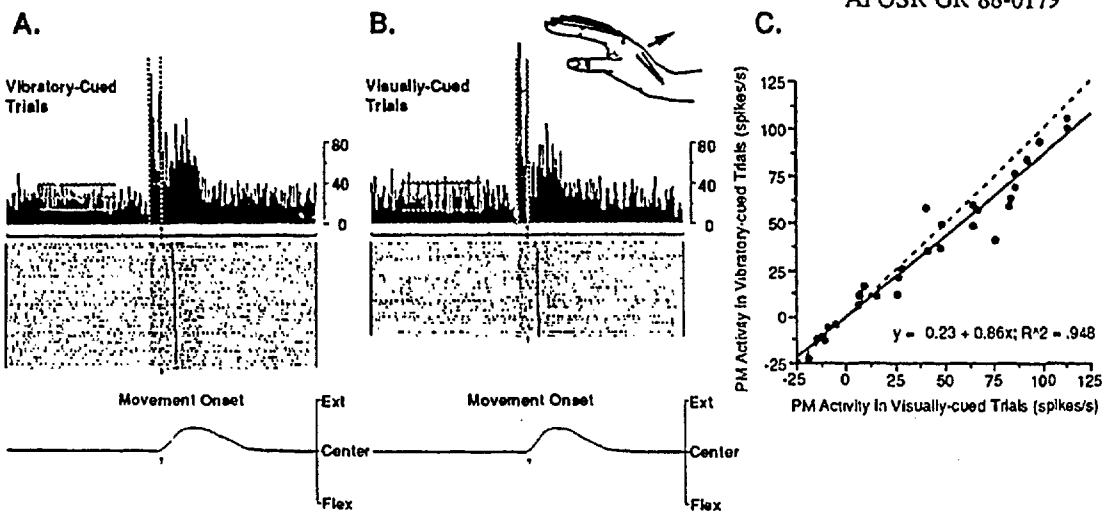


Figure 3. (A&B) General panel description as in Figure 2. In addition, left horizontal lines indicate upper and lower thresholds and mean background activity, measured while the monkey held a steady wrist position. Vertical lines indicate premovement activity period, ceasing at movement onset. Associated horizontal lines indicate upper and lower thresholds and mean premovement activity. This area 1 neuron responded to passive wrist extension. (C) The magnitude of premovement activity (PM) during visually-cued extension trials plotted against the magnitude of PM during vibratory-cued extension trials for 30 area 1 cases with deep RFs. Shown is the regression (solid) line and equation for these data. Dashed line indicates unity slope. PM in vibratory-cued trials was approximately 0.86 of that during visually cued trials. The mean difference was 6.02 spikes/sec (p=.003, paired t - test) and PM began, on the average, 30 msec earlier in vibratory- as compared with visually-cued trials (p=.0005; paired t - test).

Next, the standarized data were subjected to multiple regression analysis to determine if premovement activity in vibratory cued trials was comprised of two components, a reactiviation of the vibratory response and a component related to the premovement activity expressed when vibratory stimuli were not present. This was done using the following equation:

$$\textit{Vib trial PM activity} = \textit{constant} + \alpha * \textit{vibratory responsiveness} + \beta * \textit{visual trial premovement activity} \quad (1)$$

where α represents some portion of the magnitude of the neuron's initial vibratory response, β is some portion of the premovement activity magnitude exhibited in visually cued trials, and the constant indicates the activity not accounted for by the other two terms. Because of standardization, the constants were reduced to zero. The application of this equation resulted in the coefficients listed in Table 1.

	Area 1				*Area 3b*		
Data Group	α	β	R^2	Data Group	α	β	R^2
Flex-Cut. (N=33)	0.572[a]	0.498[a]	0.654	Flex-Cut. (N=6)	-0.422[c]	0.661[b]	0.818
Flex-Deep (N=13)	0.535[a]	1.200[b]	0.846	Flex-Deep (N=10)	-0.002[c]	0.977[b]	0.951
Ext-Cut. (N=27)	0.410[a]	0.558[a]	0.755	Ext-Cut. (N=7)	0.273[c]	0.969[b]	0.847
Ext-Deep (N=23)	0.098[c]	0.946[b]	0.839	Ext-Deep (N=6)	0.016[c]	0.983[b]	0.997

Table 1. The results of regression analyses using equation 1. Listed are the relationships derived from only those neurons for which a full set of vibratory and visually cued trials was recorded. Columns list the standardized coefficients and R^2: a measure of the variance accounted for by the regression equations. Symbols. [a] = different from 0.0 and 1.0; [b] = different from 0.0 but not from 1.0; [c] = not different from 0.0 yet different from 1.0. Probability level for significance, .01.

Predicted values for the premovement activity during vibratory cued trials were derived by multiplying the recorded vibratory response and visual trial premovement activity by the coefficients listed in Table 1. Figure 4E plots the predicted values against the actual values of vibratory trials premovement activity for area 1 neurons with extension premovement activity. Figure 4F shows that there were no trends in the residuals from these calculations.

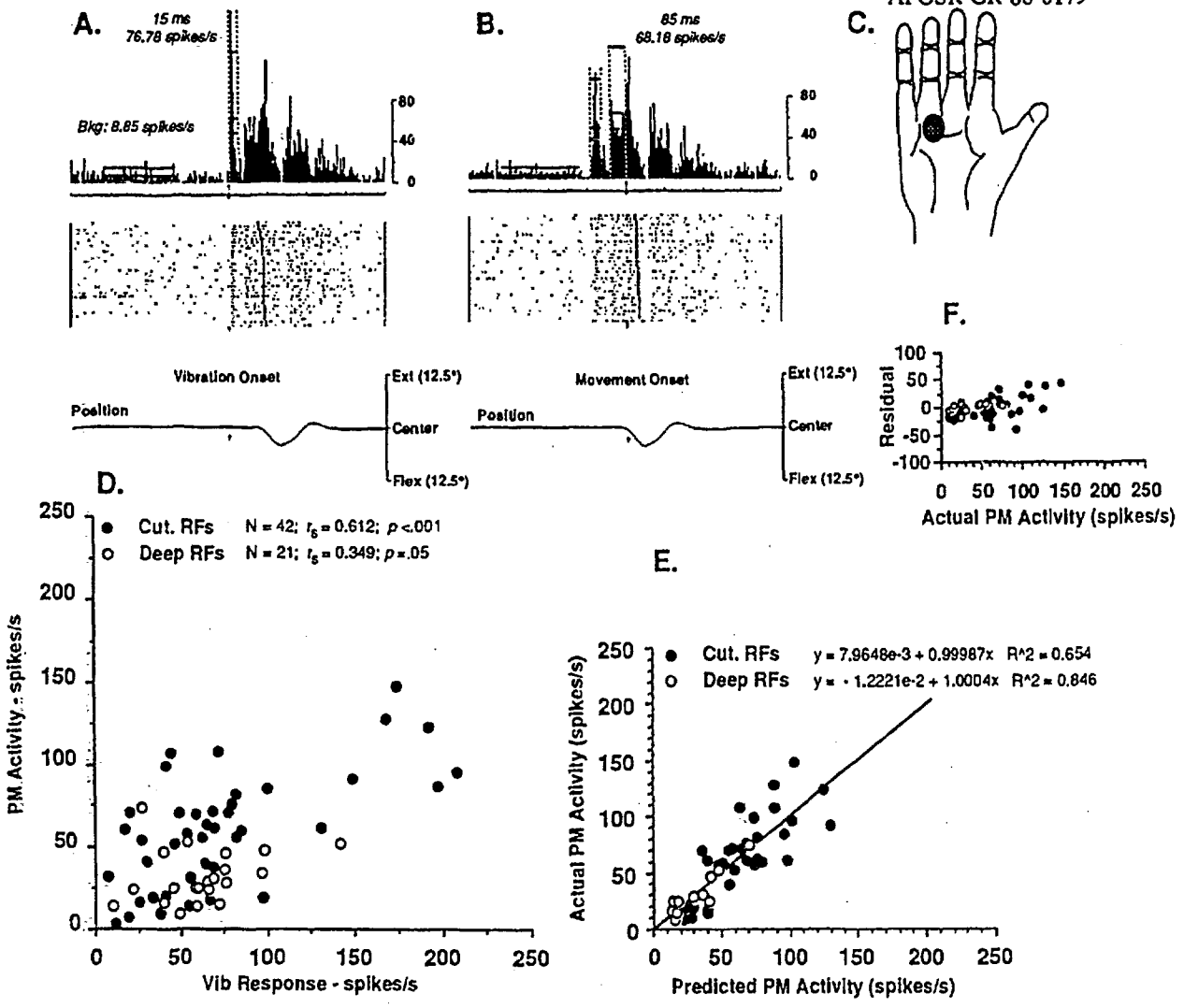


Figure 4 (A&B) Rasters, histograms of the task-related activity of an area 1 neuron along with associated average wrist position traces. (C) This neuron's cutaneous receptive field. (A) Trials centered on vibration onset and ordered by reaction time (dark marks in the rasters signify movement onset). Background activity and the stimulus-related changes in discharge rate and onset times are listed. (B) The same trials centered on movement onset. Trials ordered by movement time. The dark marks indicate reward, a 5° movement and the cessation of the vibratory stimulus. Horizontal open lines in each panel indicate the upper and lower thresholds and mean values for the background activity, vibratory response and premovement activity. Vertical dashed lines show the onset and offset of stimulus-related activity (A&B) and premovement activity (B). The full span of displays is 2 sec. (D) Scattergram of the magnitude of mean vibratory stimulus-related activity (Vib response) vs. the magnitude of the mean premovement (PM) activity for area 1 neurons, expressed in spikes/sec. Each panel indicates the number of cases analyzed, the correlation coefficient, and the probability that the correlation occurred by chance. (E) Scatterplot of the actual premovement activity (PM) recorded in vibratory-cued trials vs. the predicted PM activity obtained by using the coefficients for equation 1. Cases are separated by receptive field [illegible] direction of the movement made for area 1 neurons. Regression equations are shown in the upper right-hand corner, along with the multiple regression coefficients indicating the goodness of fit. Inset scattergram (F) plots the actual PM against the residuals remaining from the application of equation 1 to recorded values using the coefficients for equation 1. No significant trends were evident in the residuals.

These results were interpreted to indicate that the premovement activity of area 1 QA neurons is comprised of two components. The first is a reactivation of the sensory response (the peripheral component) and the second is related to the premovement activity observed when vibration is not present (presumably a central component). The peripheral component is attenuated by approximately half for all but one group (Ext-Deep), as is the central component for neurons for area 1 neurons with cutaneous RFs. The area 1 neurons with deep RFs exhibited no attenuation of the central component. Area 3b did not show sensory response reactivation, nor were the premovement activities different during the two types of sensory cued trials. This work was published during the term of AFOSR GR 88-0217.

Reference: R. J. Nelson, B. N. Smith and V. D. Douglas. Relationships between sensory responsiveness and premovement activity of quickly adapting neurons in areas 3b and 1 of monkey primary somatosensory cortex. Exp Brain Res. 84(1):75-90, 1991.

It is presently unclear what factors play a role in the differential reactivation of the peripheral sensory response for area 1 deep RF QA neurons. Two possibilities are movement direction with respect to the stimulated surface of the hand and whether a given movement is made against or assisted by a manipulandum load.

Stimulus-Response Enhancement and/or Suppression

Experiments were conducted to test the hypothesis that primary somatosensory cortical neurons are more responsive to sensory stimuli when the detection of these stimuli is important for correct behavioral performance and reward as compared with when the same stimuli only predict the reward and do not require that current behavior must be modified. Vibratory stimulus-related responses were recorded from monkey primary somatosensory cortical (SI) neurons while animals performed two tasks. In the movement task, vibratory stimuli served as the go-cue for wrist flexion or extension. In the no-movement task, movements normally made in response to vibratory stimuli were extinguished.

This study dealt with 5 area 3a, 13 area 3b and 22 area 1 neurons that had vibratory related responses in both tasks, and that had peripheral RFs related to the hand or wrist. Neurons with cutaneous and deep RFs were treated separately. All neurons in the area 3a population had deep RFs. In addition, since the stimulus-related response of a given neuron was often different as a function of the frequency of vibratory stimulation and since the vibratory responses of most neurons were sampled using more than one stimulus frequency, each sample was treated separately. However, no neuron's recordings contributed more than 6 samples to any data group.

Figure 5 illustrates the activity of an SI neuron that exhibited vibratory-related responses during movement and no-movement trials. Shown also are the neuron's receptive field (RF, Figure 5C) and the location of the recording in a drawing of a sagittal section through SI cortex (Figure 5D). This example illustrates one of the major findings of this study. Neurons in area 1 with cutaneous RFs were less responsive to vibratory stimuli during movement as compared with no-movement trials. In contrast, area 3b neurons with cutaneous RFs were more responsive during movement trials. Neurons with deep RFs had enhanced sensory responsiveness in movement as compared to no-movement trials.

An enhancement index (movement task sensory responsiveness/ movement task sensory responsiveness) was calculated for each sample by dividing the magnitude of the stimulus-related activity exhibited during movement trials by that observed during no-movement trials. The samples were grouped according to cortical location of the recorded neurons and RF type. Using movement direction as a grouping variable, either alone or in combination with cortical location and RF type, did not significantly alter the results presented below. Enhancement indices greater than 1.0 indicate that a neuron was more responsive to a vibratory stimulus when it served as the cue for movement as compared to when it did not. Conversely, enhancement indices less than 1.0 indicate that the opposite was true. Figure 5E shows the distributions of enhancement indices for the samples, grouped by cortical area and RF type. The mean enhancement index for area 1 cutaneous RF neurons was significantly different from the other four groups (one factor ANOVA; $p< 0.01$). This group had only one member for which the enhancement index was greater than 1.0. The mean enhancement indices for the remaining four groups were not significantly different from one another (one factor ANOVA; $p> 0.05$). These groups had enhancement indices distributed over larger ranges. Each of the four remaining groups had mean enhancement indices that were significantly greater than 1.0.

Using a paired t-test, the absolute value of the magnitudes of the stimulus-related activity during movement and no-movement trials were compared, grouping the samples by the same variables listed above. Area 1 neurons with cutaneous RFs had significantly smaller vibratory activities during the

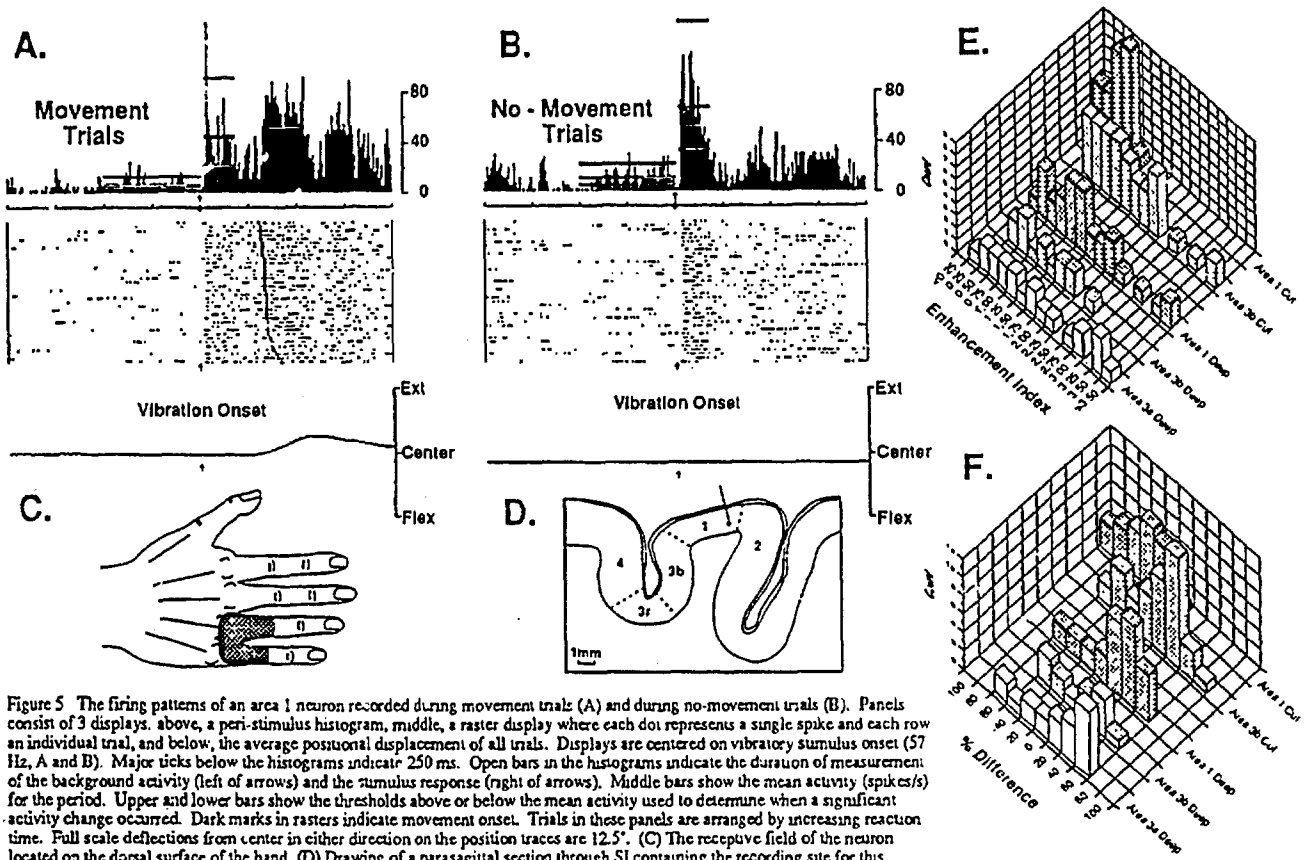


Figure 5 The firing patterns of an area 1 neuron recorded during movement trials (A) and during no-movement trials (B). Panels consist of 3 displays. above, a peri-stimulus histogram, middle, a raster display where each dot represents a single spike and each row an individual trial, and below, the average positional displacement of all trials. Displays are centered on vibratory stimulus onset (57 Hz, A and B). Major ticks below the histograms indicate 250 ms. Open bars in the histograms indicate the duration of measurement of the background activity (left of arrows) and the stimulus response (right of arrows). Middle bars show the mean activity (spikes/s) for the period. Upper and lower bars show the thresholds above or below the mean activity used to determine when a significant activity change occurred. Dark marks in rasters indicate movement onset. Trials in these panels are arranged by increasing reaction time. Full scale deflections from center in either direction on the position traces are 12.5°. (C) The receptive field of the neuron located on the dorsal surface of the hand. (D) Drawing of a parasagittal section through SI containing the recording site for this neuron. The distribution of enhancement indices (E) and the percentage differences in vibratory stimulus-related activity (F) between the movement and no-movement conditions for each neuronal recording, grouped by cortical location and receptive field type.

movement task when compared with the no-movement task (mean difference: -17.49; T=5.49; DF=25; p<.001). The vibratory responses of area 3b neurons with cutaneous RF were enhanced during movement trials (mean difference: 7.76; T=3.31; DF=38; p=.002). The vibratory activities were larger during the movement as compared with no-movement trials for deep RF neurons located in all three cortical areas. However, only the area 1 deep RF group had a mean difference in responsiveness between the two tasks that was statistically significant.

The difference in vibratory stimulus-related activity was divided by the absolute value of the larger of the two activities (movement or no-movement trial vibratory responsiveness), as an additional comparison. This gives a crude measure of the percentage change in responsiveness between the two task conditions. This was done in an attempt to standardize the difference in activity for each neuron with respect to its vibratory activity firing rate and thus reduce the greater influence that neurons with higher firing rates have on the difference calculations. The mean percentage changes of the five groups are listed in Table 2 and the distributions of these changes by group are shown in Figure 5F. Each mean percentage change was significantly different from 0.0 and paralleled the enhancement indices for the groups. On the average, area 1 neurons with cutaneous RFs were approximately 38% less responsive to vibratory stimuli when these signals were the go-cues for wrist movements. Neurons in the other four groups were more responsive to vibratory stimuli during the movement as compared with the no-movement task. The mean percentage change for the area 1 cutaneous RF neurons was significantly different from all other groups (one factor ANOVA; p< .001). These other groups, however, were not different from one another (one factor ANOVA; p> 0.05).

These results suggest that motor-set and/or selective attention may modulate the responsiveness of SI neurons to peripheral stimuli and that changes in sensory responsiveness in SI neurons differ as a function of their cortical location and RF type. Area 3a, 3b, and 1 neurons with deep receptive fields (RFs) exhibited greater stimulus-related activity during the movement task than during the no-movement task. Area 3b neurons with cutaneous RFs were similarly enhanced during the movement task, whereas area 1 neurons with cutaneous RFs were less responsive to vibratory stimuli during the movement task. This and other studies have shown that the same somatic stimulus may result in different neuronal activity depending upon the type of behavioral response that an animal has been taught to make after detecting stimulus onset. One factor that appears to differ in the two tasks is that in the movement task, the monkeys are prepared to make a movement in response to the vibration and thus may be in a different motor-set than in the no-movement condition. Others have suggested that when vibration is a cue for movement it is a relevant stimulus, whereas when vibratory stimuli are presented during no-movement they are irrelevant to the animal's behavior. This, then, would imply that there may be differences in a form of selective attention between the two tasks used in this study.

The present results suggest that changes in sensory responsiveness are somewhat specific rather than general, as might be predicted if they were due to changes in arousal or vigilance. Both enhancement and suppression of stimulus-related activity have been observed. The direction of the relative change for a given group of neurons appears to be related to their cortical location and RF type.

The role of the observed changes in sensory responsiveness is not currently known. One possibility is that cutaneous RF neurons which do not signal the characteristics of peripheral stimuli with great fidelity are suppressed during the movement task (possibly the case for the sample of area 1 neurons with cutaneous RFs). This hypothesis would seem more reasonable if it can be demonstrated that cutaneous RF neurons whose activities are entrained to the stimulus frequency or that have RFs in direct contact with the handle are not suppressed whereas those that are not entrained or have RFs away from the point of contact are less responsive in the movement task. This hypothesis is currently under investigation, yet it does not explain why the activity of deep RF neurons in area 3a, 3b and 1 and the activity of area 3b cutaneous RF neurons is enhanced during movement trials. Inputs from deep receptors may be enhanced because they signal the current limb position prior to the execution of movement and are thus behaviorally important. This work was submitted for publication published during the term of AFOSR GR 88-0217 and is currently In Press.

Reference: R. J. Nelson, B. Li, and V. D. Douglas. Sensory response enhancement and suppression of monkey primary somatosensory cortical neurons. (In Press Brain Res. Bull.)

Reward Predictability

A preliminary experiment is in progress which was designed to test the hypothesis that variations in expectation alter the sensory responsiveness and the magnitude of premovement activity exhibited by SI cortical neurons. By using a pseudo-random reward schedule for correct task performance, we sought to create a condition under which monkeys sometimes were not reinforced for seemingly appropriate movements. Several types of results were thought to be possible. In trials immediately following correct but unrewarded performance ("after trials"), both sensory responsiveness and premovement activity may be either enhanced or suppressed.

One monkey was trained to make wrist flexion and extension movements in response to vibratory go-cues, as previously described. Approximately 75% of the trials in which the monkey performed correctly were rewarded. The other 25% were not. The activity patterns of 60 task-related neurons have been recorded to date. A total of 29/60 were vibratory responsive and/or exhibited premovement activity. The distribution of unrewarded trials was determined by a pseudo-random number generator with no apparent sequential order in the output. Upon detecting the go-cue during the after trials, the monkey typically made movements in the opposite direction from the rest of the trials in that block. Neuronal activity during

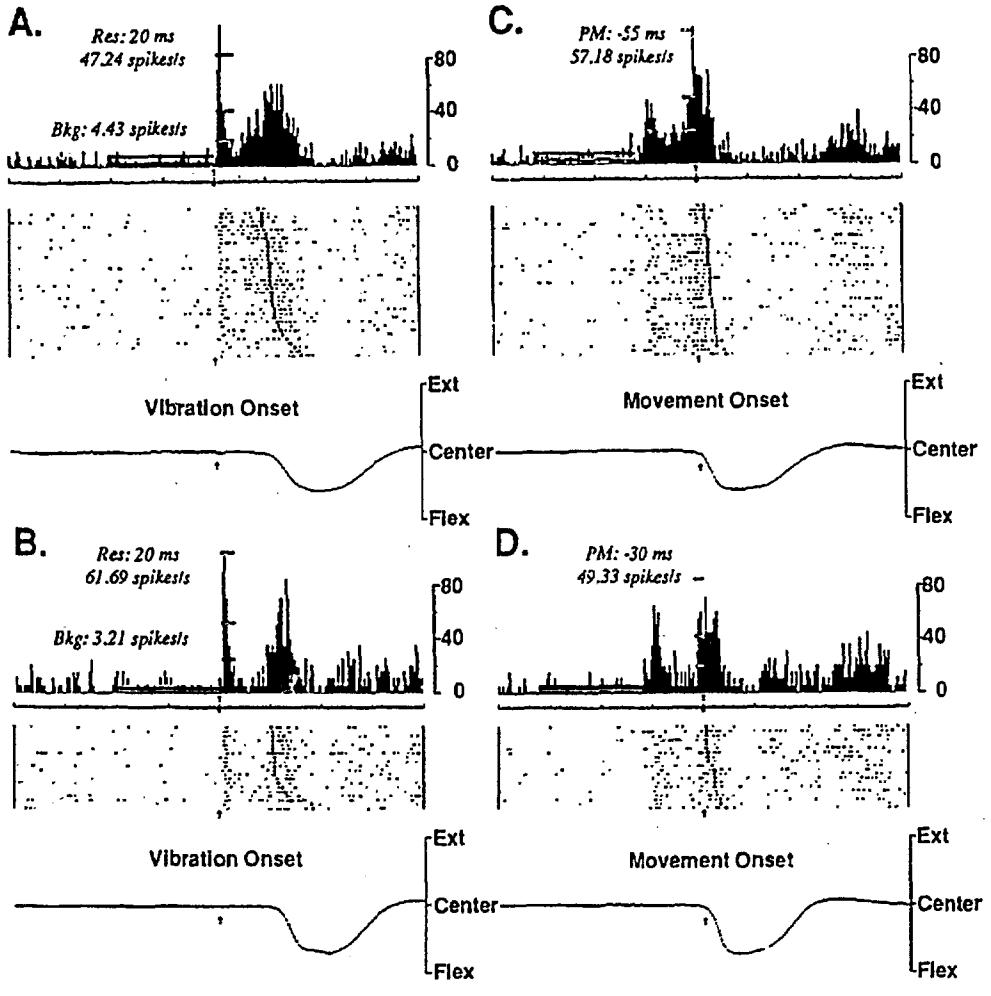


Figure 6. General description of panels as in Figure 2. The vibratory response related activity of a presumptive SI neuron for rewarded trials (A.) and after trials (B.). Traces centered on stimulus (57Hz vibration) onset. Listed are the background (Bkg) activities and the mean magnitude of the responses (Res) above background in spikes/s. Also listed are the onsets of response related activity. Panels (C.&D.) show the same trials centered on movement onset. Listed are the premovement (PM) activity magnitudes above background and their onsets before movement. This neuron was more responsive to vibration in the after trials than in the regular rewarded trials. The premovement activity was smaller in the after trials as compared with the regular rewarded trials.

rewarded flexion trials was compared with that for after trials in which the monkey also flexed his wrist (see e.g. Figure 6). Corresponding rewarded and after extension trials were also compared.

The recordings were separated into individual "cases" for several reasons. First, the activity of many neurons was studied based on the use of more than one vibratory stimulus frequency. The stimulus-related and premovement activity changes of these neurons were not always identical during blocks of trials at different stimulus frequencies. Second, two different movements were required. Flexion movements were made against a load, whereas extension movements were assisted by the same load. A case was defined as the recordings from a neuron using only one vibratory stimulus and requiring a movement in one direction. This separation resulted in a total of 88 cases from the 41/72 neurons which, because of their stereotaxic location, are believed to be located in SI. No single neuron's data contributed more than 4 cases to the data population. Confirmation of the neurons' locations awaits the histological preparation of the tissue.

To date, the vibratory stimulus-related responses and/or premovement activity magnitudes have been calculated for all 41 neurons. The activity patterns of one of these neurons can be seen in Figure 6. Sufficient trials in both task conditions were recorded for 17 cases (from 11/41 neurons) that were

vibratory responsive. The vibratory response for the rewarded trials was compared to the vibratory response during the after trials for each case. A paired *t*-test was conducted to determine if the neurons were more vibratory responsive in one type of trial as compared with the other. During the rewarded trials, the neurons as a population were less responsive to vibratory stimuli as compared with during the after trials (Mean difference: -5.939 spikes/s; t=-1.958; p<.05; one-tailed). The premovement activities for the two types of trials (after and rewarded) were also compared. When the total population of 80 premovement activity cases was analyzed (some neurons had both a stimulus response and premovement activity), the population pre-movement activities under the rewarded and after conditions were not significantly different (DF=79; Mean difference: 2.323 spikes/s; t=1.397; p=.083) . The data were subjected to an analysis of variance which resulted in the population being split into two groups. First, the ratio of the premovement activity in rewarded as compared with after trials was calculated for each case. The first group consisted of 68 cases (from 33 neurons). The records of each case in this group showed premovement facilitation or increased activity prior to movement onset. For this group, the premovement activity during rewarded trials was greater than during after trials (DF=67; Mean ratio: 1.112; t=-2.731; p=.0081). There was a linear relationship between the activity in rewarded and after trials for this group (after trail premovement activity = 0.827 x rewarded trail premovement activity +7.103 spikes/sec; r^2=.741, p<.0001). The second group consisted of 12 cases (from 7 neurons). The records of each case in this group showed premovement suppression or decreased activity prior to movement onset. For this group, the premovement activity during rewarded trials also much greater than during after trials (DF=11; Mean ratio: 1.355; t=1.355; p>.20). There was also a linear relationship between the activity in rewarded and after trials for the second group (after trail premovement activity = 0.904 x rewarded trail premovement activity - 0.949 spikes/sec; r^2=.66, p=.0013). These results suggest that premovement activity is decreased in trials when the reward predictability is decreased.

We have previously hypothesized that premovement activity represents a gating signal that suppresses peripheral inputs prior to movement. If this is true then it is reasonable to suggest that peripheral inputs are not as strongly gated when behavioral conditions become unpredictable and thus allows for more inputs to be processed. It should be restated that these experiments are currently being conducted, that the sample size is small, and the cortical locations of the recorded neurons are unconfirmed.

From these preliminary observations, it appears that during behavior, when the outcome is predictable (i.e., when the monkey has previously been rewarded for performing correctly) both sensory responsiveness and premovement activity in SI neurons are at one level. In trials which follow the withholding of the reward for correct performance, and hence the outcome is unpredictable, sensory responsiveness is enhanced. Premovement activity is also enhanced under the unpredictable condition for many neurons and suppressed for others. This suggests that during behavior with a predictable outcome, neuronal responsiveness to stimulus-related peripheral inputs is partially attenuated. When behavioral conditions become unpredictable, premovement activity (which, depending upon the time of its occurrence in relationship to EMG onset may reflect either central or peripheral inputs) is suppressed or enhanced. Further experimentation is needed to determine if cortical location, premovement activity onset timing and RF type are important factors determining the effects of reward predictability upon neuronal responsiveness in SI. We have previously hypothesized that premovement activity represents a gating signal that suppresses peripheral inputs prior to movement. If this is true then it is reasonable to suggest that peripheral inputs are not as strongly gated when behavioral conditions become unpredictable and thus allows for more inputs to be processed. It should be restated that these experiments are currently being conducted, that the sample size is small, and the cortical locations of the recorded neurons are unconfirmed.

These observations suggest the following working hypotheses. Sensory responses are elevated during unpredictable behavior conditions so that a greater amount of sensory information can be processed, lest

important inputs not be detected. Prior to movement in the after trials, premovement activity (which may contribute to the gating out of extraneous inputs) is elevated, in some neurons, to keep unimportant inputs from interfering with the monitoring of that movement. In other neurons, the premovement activity may be suppressed. It will be important to know if premovement activity for this group routinely occurs after EMG onset because this activity, if it occurs late, may actually reflect peripheral inputs that are attenuated. These thoughts are in keeping with our previous suggestions about the role of premovement activity and shed new light on the nature of enhancement and suppression of sensory responsiveness as they occur under different behavioral conditions.

Reaction Times for Wrist Movements - Ballistic Movements

Reaction times were determined for monkeys and humans who made wrist flexion and extension movements in response to vibratory and visual cues. Humans initiated movements approximately 50 msec sooner in response to vibratory as compared to visual cues (Figure 7A). For monkeys, this difference was approximately 100 msec (Figure 7B). Mean daily reaction times for monkeys and humans improved with practice until they reached a steady level of performance. Increased differences between vibratory and visual reaction times were weakly correlated with increased age of humans. The increase in the differences appeared to result from decreased reaction times by older subjects for vibratory cued movements while reaction times for visually cued movements did not consistently vary across the age range of subjects tested (19-36 yr). The results obtained using this novel paradigm suggest that it may be a useful tool for simultaneously testing behavioral performance or neurological function during somatosensorimotor and visuomotor tasks. This work was published during the term of AFOSR GR 88-0217.

Reference: R. J. Nelson, C. A. McCandlish and V. D. Douglas. Reaction times differ for hand movements in response to visual vs. vibratory cues. Somatosensory and Motor Research 7:337-352, 1990.

Reaction Times for Wrist Movements - Targeted Movements

A human RT study was carried out to test the hypothesis that wrist movements made from a centered position to acquire a visual target would occur more quickly if, in addition to the illumination of the target, subjects also received a vibratory stimulus, indicating that a movement should be made. Nine human subjects made movements from a centered wrist position to a target 5° from the center position by either flexing or extending the wrist of their preferred hand. Two go-cues were used to indicate that a movement should begin. The first consisted of illuminating a target LED on the visual display that would be illuminated if the subject made a 5° movement in the appropriate direction. The second consisted of the target *and* a vibratory stimulus delivered to the palm of the hand that was to be moved.

The RTs and MTs for small (5°) controlled movements were measured. Subjects were initially told that they should make flexion or extension movements as quickly as possible from a centered wrist position to a position indicated by target LEDs (target acquisition). These LEDs were part of the visual display described below (Experimental Design). Subjects were instructed not to sacrifice position accuracy for movement speed. They were also told that, while they would always be presented with a target indicating in what direction and how far they should move, sometimes the illumination of the target would be accompanied by vibration of the handle in which their hand rested. Combined cue and visual only trials were presented randomly in each block of 10 trials. The movement direction was alternated from block to block beginning with a request for flexion movements.

Daily mean RTs and MTs were calculated from 360 extension and 360 flexion trials that subjects ran during each session. Each subject performed the paradigm for 14 days. Figure 8A shows the average daily mean RTs for each training day. These were calculated by averaging the daily mean RTs for all subjects for a given training day. Daily RTs for combined cues trials for either movement direction were always significantly faster ($p<.01$; paired two tailed t-test) than the corresponding trials cued by the target alone (visual only). The daily differences in RTs for corresponding movements are shown in Figure 8B

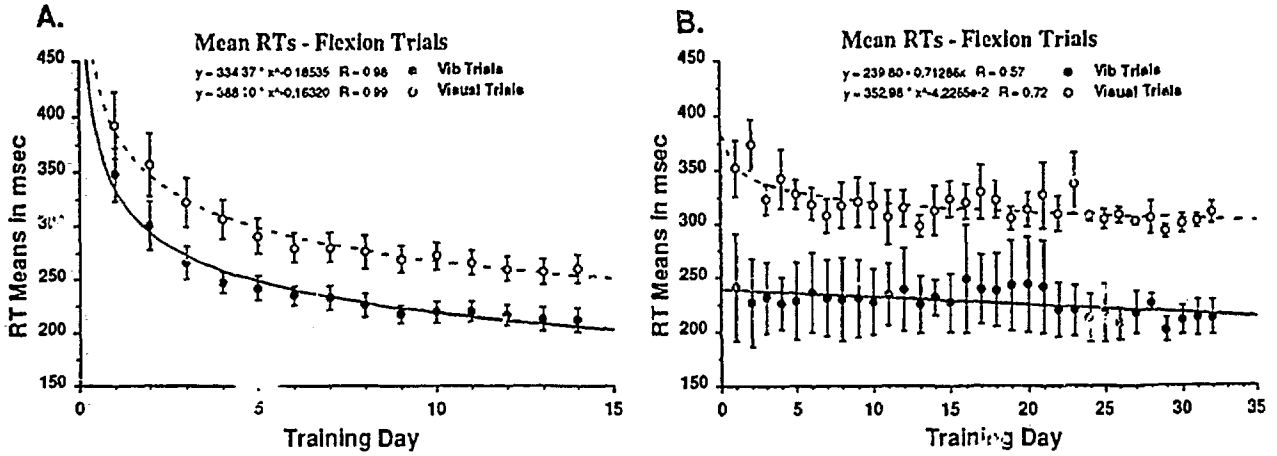
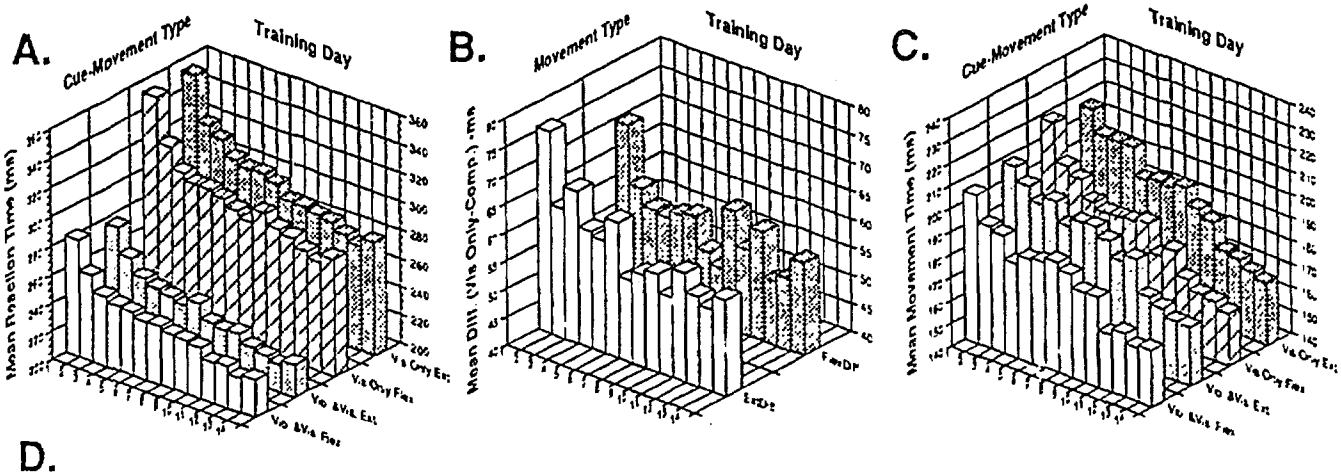


Figure 7. (A) The daily mean RTs for 11 human subjects as a function of training day for flexion trials. (B) The daily mean RTs for 4 monkeys as a function of training day for flexion trials. Shown are the best fit log and linear functions and their coefficients for these data. Solid lines indicate the fit of these data for vibratory cued trials, dashed lines indicate the fit for visually cued trials. Bars indicate standard errors of the means. With increased training the RTs improved and there was a decrease in the variability as shown by the decrease in the standard errors.

and ranged from 50-70 ms. The differences in RTs became less with practice; i.e., more days of training. MTs also improved with training (Figure 8C). However, the MTs for the four cue-movement groups were never significantly different on a given training day. The daily mean RTs and MTs from each subject for the last 5 training days were used to calculate each subject's final means. These final means were used to calculate grand average RTs and MTs (Figure 8D). The differences in the grand average RTs were calculated by subtracting the grand average RTs for the combined cue trials from those for trials using the visual cue only. These differences were approximately 53 msec in favor of the combined cue trials and were significantly different ($p<.01$; unpaired two tailed t-test).

The final mean RTs from the 11 subjects who performed the 5° fixed amplitude target paradigm were compared with the final RTs recorded from ten subjects that made ballistic movements (i.e., amplitude not restrained but >5°) in response to either vibratory or visual cues. The vibratory cued RTs from the ballistic paradigm were compared with the combined cue RTs from the target paradigm. The visually cued RTs from the ballistic paradigm were compared with the target only RTs from the target paradigm. When vibration was present, the RTs in the target paradigm were approximately 20 ms slower than in the ballistic paradigm. When vibration was not used as a cue (visual only trials), the RTs for the target paradigm were approximately 30 ms slower than in the ballistic paradigm.

Movements to acquire a target are made more quickly if a vibratory go-cue is presented in addition to the illumination of the target. Previously we have shown that ballistic movements are made more quickly in response to vibratory as compared with visual go-cues. The differences in RTs observed in these previous experiments also appear to occur when instead of unrestrained movement, subjects must make controlled movements of small amplitude. Once controlled movements are begun, the time to target acquisition (movement time) does not vary significantly regardless of whether low amplitude vibration is present or absent. Increased practice shortens RTs and MTs. Vibratory stimuli in addition to other visual cues could significantly increase performance as measured by shorter RTs. It remains to be determined whether vibratory go-cues are beneficial in situations requiring more precise movement control.



D.

Target Paradigm

	Flexion		Extension	
	Visual & Vib	Visual Only	Visual & Vib	Visual Only
RTs	234.44	287.88	231.71	285.09
MTs	175.39	176.67	177.72	178.33
DIFF	53.44*		53.38*	

Ballistic Paradigm

	Flexion		Extension	
	Vib Only	Visual Only	Vib Only	Visual Only
RTs	208.08	255.63	205.07	250.91
DIFF	47.55*		45.84*	

Paradigm Differences in RTs

Flexion		Extension	
Vis-Vib vs. Vib Only	Vis Only vs Vis Only	Vis-Vib vs Vib Only	Vis Only vs. Vis Only
26.36*	32.25*	26.64*	34.14*

*:$p<.01$; unpaired t-test

Figure 8. (A) The mean RTs by training day, separated by cue-movement type. (B) The differences in mean RTs for extension and flexion movements calculated by subtracting the mean RTs for the visual & vibratory cued trials from the mean RTs for visual cue only trials. (C) The mean MTs by training day, separated by cue-movement type. (D) The final RTs and MTs for the target paradigm and for the ballistic movement paradigm. Shown also are the differences in RTs for corresponding cue-movement types for the two paradigms.movement types for the two paradigms.

Experiments are currently being conducted in which subjects are required to make targeted movements to a 4°, 8° or 12° target. These different amplitude movements are required in a pseudorandom order within blocks of flexion or extension trials. Preliminary results from 4 subjects indicate that the same performance benefit (e.g., faster RTs with vibratory go cues) is present when subject receive variable amplitude rather than fixed targets. MTs, movement accuracy and percentage correct trials appear to be similar regardless of cue type (visual only as compared with visual plus vibratory).

List of Work Published During and Pertaining to AFOSR GR 88-0179

R.J. Nelson. Set related and pre-movement related activity in primate primary somatosensory cortical neurons depends upon stimulus modality and subsequent movement. Brain Res. Bull. 21(3):411-424, 1988.

R. J. Nelson and V. D. Douglas. Changes in premovement activity in primary somatosensory cortex differ when monkeys make hand movements in response to visual vs. vibratory cues. Brain Res. 484:43-56, 1989.

R. J. Nelson, C. A. McCandlish and V. D. Douglas. Reaction times differ for hand movements in response to visual vs. vibratory cues. Somatosensory and Motor Research 7:337-352, 1990.

R. J. Nelson, B. N. Smith and V. D. Douglas. Relationships between sensory responsiveness and premovement activity of quickly adapting neurons in areas 3b and 1 of monkey primary somatosensory cortex. Exp Brain Res. 84(1):75-90, 1991.

R. J. Nelson, B. Li, and V. D. Douglas. Sensory response enhancement and suppression of monkey primary somatosensory cortical neurons. (In Press Brain Res. Bull.)

List of Abstracts Published During and Pertaining to AFOSR GR 88-0179

R. J. Nelson and V. D. Douglas. Quantitative differences in premovement activity of primary somatosensory cortical neurons during visual versus vibratory cued hand movements. Neuroscience Abst. 14:716, 1988.

R. J. Nelson and V.D. Douglas. Differences in sensorimotor integration in cortical areas 3b and 1 of the monkey. Neuroscience Abst. 15:659, 1989.

V. D. Douglas, C. A. McCandlish and **R.J. Nelson.** Reaction times differ when humans and monkeys make hand movements in response to visual as compared to vibratory cues. Neuroscience Abst. 15:729, 1989.

R. J. Nelson and V. D. Douglas. Responsiveness of primary somatosensory cortical neurons to vibratory stimuli during movement vs. no-movement tasks. Neuroscience Abst. 16:1081, 1990.

Presenatations

Workshop Organizer "Sensory responsiveness varies as a function of the behavioral state under which stimuli are presented". Winter Conference on Brain Research - 1989.

"Set and the Single Neuron: Changes in Sensory Responsiveness in Primary Somatosensory Cortex." May 28, 1991. Hahnemann University, Philadelphia, PA.

Associated Personnel

Vickie D. Douglas, Research Assistant was be responsible for most aspects of the training and testing of animals under the close supervision of of the P.I. Ms Douglas worked for most of the three year duration of this grant and has became an indispensible member of the laboratory. She was capable of doing all data analysis and most facets of the work conducted in the laboratory including the testing of human subjects. In March of 1991, Ms. Douglas moved to Miami, FL.

John M. Denton, Research Assistant was hired to replace Ms. Douglas. A previous employee of Memphis Pathology Laboratories, Mr. Denton is fast becoming familiar with the requirements of the laboratory and shows promise of being a highly competent independent worker.

Interactions

Meetings Attended

Society for Neuroscience Annual Meetings:
- 1988 - Toronto, Ontario, Canada Nov. 12-18
- 1989 - Phoenix, AZ Oct. 29 - Nov. 3
- 1990 - St. Louis, MO Oct. 28 - Nov. 2

Winter Conference on Brain Research:
- 1989 - Snowbird, Utah Jan 21-28
- 1990 - Snowmass, CO Jan. 27-Feb. 3
- 1991 - Vail, CO Jan. 26-Feb. 2

Ad Hoc Reviewer

National Science Foundation
Veteran's Adminitration
Journal of Neurophysiology
Brain Research Bulletin
Physiology and Behavior
NIH Program Project Grant Site Visit Team - Mar-Apr 1989
NIH Special Review Panel - Mar-Apr 1989

Dissertation Commitee Member

Carl McCandlish, University of Tennessee, Memphis - 1990-present

Postdoctoral Trainee

Thomas W. Gardiner, Ph.D. - June 1988 to March 1990

New Discoveries

-none-